

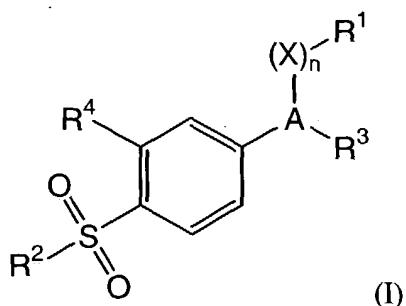
WHAT IS CLAIMED IS:

1. A pharmaceutical dosage form comprising a fill material sealed in capsule shells wherein the fill material comprises (a) a selective cyclooxygenase-2 inhibitory drug of low water solubility and (b) at least one pharmaceutically acceptable sulfite compound, wherein the capsule shells comprise gelatin, and wherein the at least one pharmaceutically acceptable sulfite compound is present in a total sulfite amount sufficient to inhibit gelatin cross-linking and/or pellicle formation in the capsule shells upon storage of the dosage form.
2. The dosage form of Claim 1 wherein the at least one pharmaceutically acceptable sulfite compound is selected from the group consisting of sodium metabisulfite, sodium bisulfite, and sodium thiosulfate.
3. The dosage form of Claim 1 wherein the at least one pharmaceutically acceptable sulfite compound is present in a total sulfite amount of not more than about 10% of the dosage form on a dry weight basis.
4. The dosage form of Claim 1 wherein the fill material further comprises at least one pharmaceutically acceptable excipient selected from the group consisting of free radical-scavenging antioxidants, sweeteners, preservatives, wetting agents, buffering agents, flavoring agents, colorants, stabilizers, fragrances, glidants, crystallization inhibitors, adhesives, lubricants, and thickeners.
5. The dosage form of Claim 1 further comprising at least one free radical-scavenging antioxidant compound selected from the group consisting of α -tocopherols, ascorbic acids, ascorbates, palmitates, butylated hydroxyanisoles, butylated hydroxytoluenes, fumaric acids, fumarates, hypophosphorous acids, malic acids, and alkyl gallates.
6. The dosage form of Claim 5 wherein the at least one free radical-scavenging antioxidant is present in a total antioxidant amount of about 0.01% to about 5% of the dosage form on a dry weight basis.
7. The dosage form of Claim 1 further comprising at least one sweetener compound selected from the group consisting of mannitols, propylene glycols, sodium saccharins, acesulfame Ks, neotames, and aspartames, sorbitols, sucroses, and

high-fructose corn syrups.

8. The dosage form of Claim 1 wherein the fill material further comprises at least one preservative compound selected from the group consisting of benzalkonium chlorides, benzethonium chlorides, benzyl alcohols, chlorobutanol, phenols, phenylethyl alcohols, phenylmercuric nitrates, and thimerosal.
9. The dosage form of Claim 1 wherein the fill material further comprises at least one surfactant selected from the group consisting of benzalkonium chlorides, benzethonium chlorides, cetylpyridinium chlorides, dioctyl sodium sulfosuccinates, nonoxynol 9, nonoxynol 10, octoxynol 9, poloxamers, polyoxyethylenes (8), caprylic monoglycerides, capric monoglycerides, caprylic diglycerides, capric diglycerides, polyoxyethylene (35) castor oils, polyoxyethylene (20) cetostearyl ethers, polyoxyethylene (40) hydrogenated castor oils, polyoxyethylene (10) oleyl ethers, polyoxyethylene (40) stearates, polysorbate 20s, polysorbate 40s, polysorbate 60s, polysorbate 80s, propylene glycol laurates, sodium lauryl sulfates, sorbitan monolaurates, sorbitan monooleates, sorbitan monopalmitates, sorbitan monostearates, and tyloxapol.
10. The dosage form of Claim 1 wherein the fill material is liquid.
11. The dosage form of Claim 1 wherein the fill material is self-emulsifying upon contact with gastric fluid.
12. The dosage form of Claim 1 wherein the fill material further comprises a solvent.
13. The dosage form of Claim 12 wherein the selective cyclooxygenase-2 inhibitory drug and the at least one pharmaceutically acceptable sulfite compound are in solution in the solvent.
14. The dosage form of Claim 12 wherein the solvent is present in an amount of about 5% to about 95% of the dosage form on a dry weight basis.
15. The dosage form of Claim 12 wherein the solvent comprises at least one of a glycol component and a glycol ether component.
16. The dosage form of Claim 12 wherein the solvent comprises a glycol ether component having an average molecular weight of about 75 to about 1000.

17. The dosage form of Claim 12 wherein the solvent comprises at least one glycol ether selected from the group consisting of ethylene glycol monomethyl ethers, ethylene glycol dimethyl ethers, ethylene glycol monoethyl ethers, ethylene glycol diethyl ethers, ethylene glycol monobutyl ethers, ethylene glycol dibutyl ethers, ethylene glycol monophenyl ethers, ethylene glycol monobenzyl ethers, ethylene glycol butylphenyl ethers, ethylene glycol terpinyl ethers, diethylene glycol monomethyl ethers, diethylene glycol dimethyl ethers, diethylene glycol monoethyl ethers, diethylene glycol diethyl ethers, diethylene glycol divinyl ethers, ethylene glycol monobutyl ethers, diethylene glycol dibutyl ethers, diethylene glycol monoisobutyl ethers, triethylene glycol dimethyl ethers, triethylene glycol monoethyl ethers, triethylene glycol monobutyl ethers, and tetraethylene glycol dimethyl ethers.
18. The dosage form of Claim 12 wherein the solvent comprises at least one glycol selected from the group consisting of propylene glycols, 1,3-butanediol and polyethylene glycols.
19. The dosage form of Claim 12 wherein the solvent comprises polyethylene glycol having an average molecular weight of about 100 to about 10,000.
20. The dosage form of Claim 12 further comprising at least one co-solvent selected from the group consisting of alcohols, oleic acid triglycerides, linoleic acid triglycerides, caprylic triglycerides, capric triglycerides, caprylic monoglycerides, capric monoglycerides, caprylic diglycerides, capric diglycerides, polyoxyethylene caprylic glycerides, polyoxyethylene capric glycerides, propylene glycol fatty acid esters, polyoxyethylene (35) castor oils, polyoxyethylene glyceryl trioleates, lower alkyl esters of a fatty acid, and water.
21. The dosage form of Claim 1 wherein the selective cyclooxygenase-2 inhibitory drug is a compound of formula (I)



wherein:

A is a substituent selected from partially unsaturated or unsaturated heterocyclyl and partially unsaturated or unsaturated carbocyclic rings, preferably a heterocyclyl group selected from pyrazolyl, furanonyl, isoxazolyl, pyridinyl, cyclopentenonyl and pyridazinonyl groups;

X is O, S or CH₂;

n is 0 or 1;

R¹ is at least one substituent selected from heterocyclyl, cycloalkyl, cycloalkenyl and aryl, and is optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxy carbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

R² is methyl, amino or aminocarbonylalkyl;

R³ is one or more radicals selected from hydrido, halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocyclyloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclyl, cycloalkenyl, aralkyl, heterocyclalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxy carbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxy carbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-aryl amino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-aryl amine, aminoalkyl, alkylaminoalkyl, N-aryl aminoalkyl, N-aralkylaminoalkyl, N-alkyl-N-aralkylaminoalkyl, N-alkyl-N-aryl aminoalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-arylaminosulfonyl, arylsulfonyl and N-alkyl-N-

arylaminosulfonyl, R³ being optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxy carbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio; and R⁴ is selected from hydrido and halo.

22. The dosage form of Claim 1 wherein the selective cyclooxygenase-2 inhibitory drug is selected from the group consisting of celecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, 2-(3,5-difluorophenyl)-3-[4-(methylsulfonyl)phenyl]-2-cyclopenten-1-one, 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3-(2H)-pyridazinone, and pharmaceutically acceptable salts and prodrugs thereof.
23. The dosage form of Claim 1 wherein the cyclooxygenase-2 inhibitory drug is celecoxib.
24. The dosage form of Claim 23 wherein the celecoxib is present in an amount of about 10 to about 400 mg.
25. The dosage form of Claim 1 wherein the capsule shells are hard gelatin capsule shells.
26. The dosage form of Claim 1 wherein the capsule shells are soft gelatin capsule shells.
27. The dosage form of Claim 1 wherein each of the gelatin capsule shells have a fill capacity of about 0.1 ml to about 2 ml.
28. The dosage form of Claim 1 wherein the capsule shells and/or the fill material further comprise at least one substance that promotes cross-linking of gelatin when in contact therewith, said substance being the selective cyclooxygenase-2 inhibitory drug or an excipient substance, and said substance acting independently or in combination with one or more other substances to promote said cross-linking.
29. The dosage form of Claim 28 comprising a first said capsule shell and said fill material and a second said capsule shells and said fill material, said first and second capsule shell and fill material being substantially identical; wherein upon

- (a) testing the first capsule shell and fill material in a first *in vitro* dissolution assay;
- (b) storing a second capsule shell and fill material in a closed container maintained at 40 °C and 85% relative humidity for a period of four weeks; and, after said storage,
- (c) testing the second capsule shell and fill material in a second *in vitro* dissolution assay which is identical to the first *in vitro* dissolution assay; the amount of the cyclooxygenase-2 inhibitory drug dissolved at 45 minutes in the second dissolution assay is within ± 15 percent of the amount of cyclooxygenase-2 inhibitory drug dissolved at 45 minutes in the first dissolution assay; and wherein the first *in vitro* dissolution assay is conducted within a reasonably short time after formation of the dosage form.

30. The dosage form of Claim 1 wherein the at least one pharmaceutically acceptable sulfite compound is sodium metabisulfite and/or sodium bisulfite in a total sulfite amount of about 0.5% to about 5% on a dry weight basis; wherein the fill material further comprises hydroxypropyl methylcellulose and/or polyethylene glycol, wherein the selective cyclooxygenase-2 inhibitory drug is celecoxib present in an amount of about 10 to about 400 mg, and wherein the capsule shells are soft gelatin capsule shells.